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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,051	03/24/2005	Sek Chung Fung	12279-169-999	1772

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,051	FUNG, SEK CHUNG	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/02/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communications filed 02 July, 2008, and 05 August, 2008. Claims 41-54 are pending in the instant application.

37 C.F.R. § 1.98

The information disclosure statement filed 02 July, 2008, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 54 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. The claim is directed toward an anti-CD4 Mab designated 5A8. The disclosure fails to provide any guidance pertaining to the origins of this Mab, appropriate structural

information, or deposit information. However, the prior art identifies at least one anti-CD4 Mab that has been designated 5A8 (Burkly *et al.*, 1995). It is not readily manifest if the claim references this antibody or an entirely different antibody. Appropriate clarification is required.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Biological Deposit Requirement

Claim 54 is rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure for the claimed invention. It is apparent that the monoclonal antibody 5A8, as well as its attendant hybridoma cell line, are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the hybridoma cell lines producing said antibodies. See 37 C.F.R. § 1.802.

Due to the unpredictability associated with antibody production (i.e., each antibody generally has a unique structure) and the failure of the specification to provide any detailed structural information concerning the claimed antibody,

Mabs 5A8 does not appear to be a readily available material.[1] Deposit of the hybridoma cell line producing said antibody or detailed structural information (i.e., the complete nucleotide or amino acid sequence of each antibody) would satisfy the enablement requirements of 35 U.S.C. § 112. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty **and** that **all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements.** See 37 C.F.R. § 1.808.

If the deposits have not been made under the provisions of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of the application, access to the deposits will be afforded to one determined by the Commissioner to be entitled thereto;

1 It has been well-documented that most animals are capable of producing a vast repertoire of structurally and functionally distinct antibodies. For instance, conservative estimates suggest that humans are capable of producing over 32 million different combinations of light and heavy chains. This estimate excludes various other sources of diversity. See "Immunoglobulins: Molecular Genetics", in *Fundamental Immunology, Fourth Edition*, W. E. Paul, ed., Lippincott-Raven Publishers, Philadelphia, 1999, pp. 142-143.

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposits will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 C.F.R. § 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 C.F.R. § 1.809(d) should be added to the specification. See 37 C.F.R. § 1.803-1.809 for additional explanation of these requirements. Applicant is reminded that if a deposit is made according to the terms of the Budapest Treaty the response still needs to contain a statement specifying that **all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.**

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said

subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The previous rejection of claims 41-53 under 35 U.S.C. § 103(a) as being unpatentable over Johnson *et al.* (2002) and Hanna *et al.* (2000), is hereby withdrawn in view of the new grounds of rejection set forth below.

Claims 41-50 and 52-54 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Burkly *et al.* (1995) and Nagashima *et al.* (2001). The claims are directed toward a method of preventing the infection of HIV-1 target cells by administering an anti-CD4 antibody and gp41 polypeptide inhibitor, wherein said compounds display synergistic inhibitory activity toward HIV. Additional limitations concerning the peptide, dosing, and assay methods are also claimed. Burkly and colleagues examined the ability of an anti-CD4 Mab, designated 5A8, to synergize with Mabs against anti-HIV-1 gp120. The authors reported that Mab 5A8 presumably inhibits HIV-1 entry by affecting a postbinding membrane fusion event. This study clearly demonstrated that Mab 5A8 is capable of acting in a synergistic manner with a number of different anti-gp120 antibodies. (see Abstract, p. 4267). This teaching also employed PBMC-based cell assays and the detection of p24. This reference does not disclose a method involving the administration of both an anti-CD4 antibody and a gp41 polypeptide inhibitor. However, Nagashima and associates examined the synergistic activity of a composition comprising a gp41 polypeptide fusion inhibitor (e.g., T-20) and CD4-IgG fusion protein (PRO 542). PRO 542 functions as an attachment inhibitor. The inclusion of both of these compounds produced synergistic inhibitory effects (see

abstract, p. 1121). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize two known antivirals to inhibit HIV replication. The courts have previously concluded that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. *In re Kerkhoven*, 626 F.2d 846, 850, 205 U.S.P.Q. 1069, 1072 (C.C.P.A. 1980) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be *prima facie* obvious.). See also *In re Crockett*, 279 F.2d 274, 126 U.S.P.Q. 186 (C.C.P.A. 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and *Ex parte Quadranti*, 25 U.S.P.Q.2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious). Moreover, there was a reasonable expectation that both of these compounds would behave synergistically if combined, since they both displayed synergistic activities when previously combined with other known antivirals. Nagashima and associates note that the multistep, interdependent nature of HIV-1 entry suggests that antiviral drug combinations might produce synergistic results (see background, p. 1121). Thus, both a reasonable expectation of success and the motivation to combine these known antivirals were present in the prior art.

Claim 51 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Burkly *et al.* (1995) and Nagashima *et al.* (2001), as applied *supra* to claims 41-50 and 52-54, and further in view of Olson *et al.* (2007).[2] The claim requires the addition of a third known antiviral agent (e.g., a nucleoside reverse transcriptase inhibitor) to the inhibitory method. Olson and coworkers clearly disclose antiviral compositions comprising an anti-coreceptor Mab (e.g., anti-CCR5) and one or **more** antiviral agents (e.g., T-20, zidovudine, etc.) (see pp. 25-26). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize an additional antiviral compound (e.g., an NRTI) along with Mab 5A8 and T-20 to inhibit HIV replication. One of ordinary skill in the art would have reasonably expected such a combination therapy to be quite effective at inhibiting HIV-1 viral replication.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the

2 Olson et al. (2007) claims priority to U.S. Provisional Application No. 60/358,886, filed 22 February, 2002.

Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

22 November, 2008